

## **REMARKS**

This amendment responds to the office action mailed June 1, 2004. Prior to entry of this amendment, claims 38-71 and 73-88 were pending and under consideration in the instant Application. With this amendment, claims 38, 73, and 81 are amended, no claims are cancelled, and new claims 89-94 are presented for consideration. Thus, following entry of this amendment, claims 38-71 and 73-94 are pending and under consideration.

Applicants kindly thank the PTO for withdrawing the previous rejections under 35 U.S.C. §§ 102 and 112.

In the discussion that follows, all references to the specification of the present application are to the published version of the application, which published as US 2002/0182592.

### **I. The Amendments to the Claims**

This paper presents an amendment to claims 38, 73, and 81 and new claims 89-94. The amendments to claims 38, 73, and 81 are fully supported by the application as filed, and thus do not present new matter. In particular, support for the amendments to claims 38, 73, and 81 may be found, for example, at in the specification at paragraphs 16, 174 and 175.

Further, support for new claims 89-91 may be found, for example, in the specification at paragraph 174. Support for new claims 92-94 may be found, for example, in the specification at paragraphs 171 and 172.

Since the amendments to claims 38, 73, and 81 and new claims 89-84 are fully supported by the application as filed and do not present new matter, Applicants respectfully request entry of the amendment to the claims under 37 C.F.R. § 1.111.

### **II. The Amendment to the Specification**

The specification has been amended to delete superfluous language, thereby improving the clarity of the description. The amendment to the specification is fully supported by the application as filed and therefore does not present new matter. In particular, support for the amendment to the specification can be found, for example, in paragraph 175 as previously pending. As the amendment to the specification is fully supported by the application as filed and does not present new matter, entry of the amendment to the specification is respectfully requested under 37 C.F.R. § 1.111.

**III. The Rejection of Claims 38-71 and 73-88  
under 35 U.S.C. § 112, Second Paragraph**

Claims 38-71 and 73-88 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the PTO contends that the term “plurality” can be interpreted to mean more than one copy of a single object or more than one kind of class of a particular object. Thus, the PTO contends that the claims are unclear because the limitations that recite the term “plurality” could refer to more than one of a single class of object or two or more classes of the object.

The legal standard for claim definiteness requires that “those skilled in the art [be able to] understand what is claimed when the claim is read in light of the specification.” *See Orthokinetics, Inc. v. Safety Travel Chairs, Inc.* 1 USPQ2d 1081, 1088 (Fed. Cir., 1986). “If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.” *See Personalized Media*, 48 USPQ2d 1880, 1888, quoting *Miles Lab., Inc. v. Shandon, Inc.* 997 F.2d 870, 238 USPQ2d 1123 (Fed. Cir., 1993).

Applicants respectfully submit that one of skill in the art can recognize the scope of the claim limitations that recite the term “plurality.” Applicants’ use of “plurality” is intended to encompass both definitions of this term identified by the PTO. For example, the claim limitation “plurality of envelope proteins” is intended to encompass multiple copies of a single envelope protein as well as multiple different envelope proteins. Similarly, the limitation “plurality of viral particles” is intended to encompass, for example, multiple copies of a single viral particle as well as multiple different viral particles. Thus, the term “plurality,” when afforded its ordinary dictionary definition, distinctly claims what Applicants regard as their invention. As such, one of skill in the art can recognize the scope of the invention as presently claimed, since the claims encompass both meanings of the term “plurality.” Applicants note that the PTO’s recognition of both meanings actually supports Applicants’ contention that the scope of this term is clear to the skilled artisan.

In view of the foregoing, Applicants respectfully submit that the rejection of claims 38-71 and 73-88 as indefinite under 35 U.S.C. § 112, second paragraph, is erroneous and should be withdrawn.

**IV. The Rejection of Claims 38-71 and 73-88 under 35 U.S.C. § 112, First Paragraph**

Claims 38-71 and 73-88 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. In particular, the PTO contends that a method that recites the terms “plurality,” “plurality of cells,” “plurality of viral particles,” and plurality of envelope proteins” is not supported by the specification in that there is no literal support for the term “plurality.” In response, Applicants respectfully submit that the rejection is moot as to the term “plurality of cells,” and that the application as filed demonstrates that Applicants were in possession of the invention as presently claimed at the time of filing. Therefore, Applicants respectfully submit that the rejection is in error and earnestly request its withdrawal.

A claim is supported by adequate written description when “the original disclosure [shows] that the inventor possessed the invention at the time of filing.” *See Moba B.V. v. Diamond Automation, Inc.* 66 USPQ2d 1429, 1439 (Fed. Cir. 2003). Possession of a claimed invention is assessed from the viewpoint of one skilled in the art. *See id.*, citing *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1563-64 (Fed. Cir. 1991). Further, “[t]he written description requirement does not require the applicant ‘to describe exactly the subject matter claimed, [instead], the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. *See Moba*, 66 USPQ2d at 1439, quoting *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 54 USPQ2d 1227, 1232 (Fed. Cir. 2002). Thus, the written description requirement of § 112 does not require that the application describe the invention using exactly the same terms as the claims.

Further, the PTO bears a *prima facie* burden of establishing by a preponderance of the evidence that one of skill in the art would not recognize from an Applicants’ disclosure the possession of a claimed invention. *See In re Wertheim*, 191 USPQ 90, 98 (CCPA 1976). In rejecting a claim for lack of adequate written description, the PTO must set forth express findings of fact that provide reasons why a person skilled in the art would not have recognized Applicants’ possession of the claimed invention at the time the application was filed. *See M.P.E.P.* § 2163(III)(A).

In rejecting claims 38-71 and 73-88 for alleged lack of written description, the PTO contends that there is no literal support for the term “plurality” either alone or in combination with the terms “cells,” “viral particles,” and “envelope proteins” in the specification as filed. For the purposes of this rejection, the PTO contends that the term “plurality” refers to two

different kinds of the claimed limitation. Even adopting *arguendo* the PTO's construction of "plurality," the PTO fails to provide any basis for why one of skill in the art would not recognize Applicants' possession of the invention as presently claimed. Therefore, the rejection should be withdrawn in view of the PTO's failure to make a *prima facie* case of non-description.

Moreover, the specification of the present application clearly indicates to one of skill in the art that Applicants were in possession of the claimed invention at the time the application was filed. As an initial matter, the PTO has objected to the term "plurality" in the absence of any other limitation. Applicants believe that the term "plurality" does not appear in the amended claims except as a "plurality of viral particles" or "plurality of envelope proteins." Both of these terms are supported by the specification.

The claim limitations "plurality of viral particles" and "plurality of envelope proteins" are supported, for example, by the specification at paragraphs 175 and 178. These paragraphs describe a method for preparing viral particles, which comprise the envelope proteins, that can be used in the methods of the invention. Paragraph 175 indicates that the patient-derived segments that encode the envelope protein can be amplified from patient serum and cloned into expression vectors. These vectors can be used to express envelope proteins in order to make viral particles that comprise the envelope proteins. Further, paragraph 175 teaches that "many (>100) independent *E. coli* transformants were pooled and ... are collectively referred to as pHIVenv." This paragraph clearly indicates to one of skill in the art that Applicants were in possession of a collection of vectors that can encode a plurality of envelope proteins. Moreover, this paragraph makes it clear that Applicants contemplated that the plurality of envelope proteins can include more than one different envelope protein, in that it would not be advantageous to pool greater than 100 independent transformants if each of the vectors encoded identical envelope proteins.

Further, paragraph 178 indicates that the pooled expression vectors, *i.e.*, pHIVenv, can be used to express envelope proteins in viral particles. Thus, this paragraph provides support for the term "plurality of envelope proteins." In addition, because the vectors can encode different envelope proteins, as described above, the vectors can also be used to express more than one different kind of envelope protein. As such, Applicants clearly contemplated a plurality of different kinds of envelope proteins. Moreover, paragraph 178 also describes preparation of viral particles that can comprise envelope proteins prepared from the pooled expression vectors, thus providing support for the term "plurality of viral

particles.” In addition, because the vectors can encode different envelope proteins, as described above, the vectors can be used to produce more than one different kind of viral particle. Thus, at the time the specification was filed, Applicants clearly contemplated a plurality of different kinds of viral particles. Therefore, one skilled in the art would clearly recognize that Applicants were in possession of the invention as presently claimed at the time the application was filed.

Finally, Applicants do not agree that the limitation “plurality of cells” is insufficiently supported by the application as filed. However, without agreeing to the propriety of the rejection as to this limitation, and solely to expedite prosecution of the claims, Applicants have deleted this limitation from the claims. Accordingly, Applicants respectfully submit that the rejection is moot as to the limitation “plurality of cells.”

In view of the foregoing, Applicants respectfully submit that the rejection of claims 38-71 and 73-88 as not described under 35 U.S.C. § 112, first paragraph, is moot in part and erroneous in part, and earnestly request its withdrawal.

#### **V. The Obviousness Rejection under 35 U.S.C. § 103(a)**

Claims 38-71 and 73-88 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Gao *et al.*, 1996, *Journal of Virology*, 70:1651-1667 (“Gao”) and Petropoulos *et al.*, 2000, *Antimicrob. Agents. Chemother.*, 44:920-928 (“Petropoulos”) in view of Grovit-Ferbas *et al.*, 1998, *Journal of Virology*, 72:8650-8658 (“Grovit”) and Trkola *et al.*, 1999, *Journal of Virology*, 73:8966-8974 (“Trkola”). In response, Applicants respectfully submit that the PTO cannot establish *prima facie* obviousness of claims 38-71 and 73-94 as presently pending in view of the combination of cited references.

##### **A. The Legal Standard**

To reject a claim under 35 U.S.C. § 103(a), the PTO bears the initial burden of showing an invention to be *prima facie* obvious over the prior art. *See In re Bell*, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1992). If the PTO cannot establish a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent. *See In re Oetiker*, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992). The PTO must meet a three-part test to render a claimed invention *prima facie* obvious.

To begin with, the prior art references cited by the PTO must provide “motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant.” *See In re Kotzab*, 55 U.S.P.Q.2d 1316 (Fed. Cir. 2000). Where one

reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See id.* Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 51 U.S.P.Q.2d 1386 (Fed. Cir. 1999). The suggestion may be found in implicit or explicit teachings within the references themselves, from the ordinary knowledge of one skilled in the art, or from the nature of the problem to be solved. *See id.*

Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). The expectation of success, like the motivation to combine two prior art references, must come from the prior art, not the applicant's disclosure. *See id.*

Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See In re Gartside*, 53 U.S.P.Q.2d 1769 (Fed. Cir. 2000). If any one of these three factors is not met, the PTO has failed to establish a *prima facie* case of obviousness and the applicant is entitled to grant of a patent without making any affirmative showing of non-obviousness.

**B. The Prior Art Provides neither Motivation to Combine the Cited References nor Reasonable Expectation of Successfully Practicing the Claimed Methods to An Artisan of Ordinary Skill**

None of the cited references, either alone or in combination, provide motivation to combine the cited references or a reasonable expectation of success to an artisan of ordinary skill for practicing the methods of the invention. First, the cited references provide no motivation to combine the assays described by Gao and Petropoulos. Second, the combination of references provides no reasonable expectation to an ordinarily-skilled artisan that the assays of Gao and Petropoulos can be successfully combined to teach the methods presently recited by the claims.

Petropoulos teaches a single-cycle transfection assay with HIV vectors that can be used, for example, to test the sensitivity or resistance of an HIV isolated from a patient sample to compounds. As noted by the PTO, Petropoulos does not teach analysis of patient-derived *env* segments, but rather focuses on HIV *gag* and *pol* genes amplified from patient samples.

Gao teaches a single-round infectivity assay using *env* genes amplified from PBMC-cultured viruses. In view of the high mutation rate of HIV, especially in the envelope region, passage through PBMC culture is very likely to introduce mutations that increase viral fitness in culture. Indeed, Gao reports that the envelope gene of one of the viruses passed through culture exhibits 1% sequence divergence from the envelope gene of the same virus from the patient sample. See Gao at page 1659, col. 2, second full paragraph. Accordingly, the envelope proteins used in the single-round infectivity assay of Gao are obtained from PBMC-cultured viruses that may exhibit altered structural and/or functional properties from the envelope proteins of viruses found in patient samples.

An artisan of ordinary skill would not be motivated to combine the assay of Gao with the method of Petropoulos since the mutations introduced in PBMC culture as described by Gao would distort the drug susceptibility or resistance phenotypes determined in an assay similar to that of Petropoulos. Further, this distortion would lead the ordinarily-skilled artisan to believe that the combination of Petropoulos and Gao would not successfully yield a method for identifying whether a population of viruses infecting a patient is resistant or susceptible to a compound or entry inhibitor, for largely the same reason. That is, culturing of viruses through PBMC culture prior to analysis can introduce mutations change the phenotype of the viral population, preventing the assay from properly reflecting the resistance or susceptibility of the viral population. Therefore, one of ordinary skill in the art would not expect to be able to successfully practice the claimed methods by combining Gao with Petropoulos, even if she were motivated to do so.

Neither of the other references cited by the PTO to provide the motivation to combine or reasonable expectation of success missing from Gao and Petropoulos. Grovit merely explores the structural and functional properties of an envelope protein isolated from an individual virus and in no way discusses any kind of single-round infectivity assay. Similarly, Trkola uses fully replication competent viruses in an antibody neutralization assay and also does not discuss a single-round infectivity assay. Therefore, neither Trkola nor Grovit provide any sort of motivation to the artisan of ordinary skill to combine the assays of Gao and Petropoulos, nor do they provide a reasonable expectation of successfully doing so. Accordingly, none of the references, either alone or in combination, provide a motivation to combine Gao with Petropoulos or a reasonable expectation of success to an artisan of ordinary skill to practice the methods of the present invention.

In view of the foregoing, Applicants respectfully submit that the PTO cannot establish *prima facie* obviousness of amended claims 38, 73, and 81. Since each of the remaining claims depends from one of such claims, all of claims 38-71 and 73-94 are also non-obvious. Accordingly, Applicants respectfully request that the rejection of claims 38-71 and 73-88 as obvious under 35 U.S.C. § 103(a) be withdrawn.

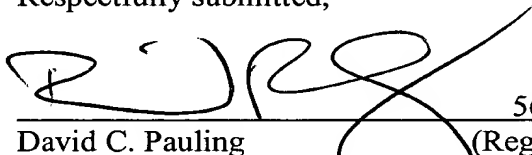
### **CONCLUSION**

In light of the above amendments and remarks, Applicants respectfully submit that claims 38-71 and 73-94 satisfy all the criteria for patentability and are in condition for allowance. Applicants respectfully request that the Examiner reconsider this application with a view towards allowance and solicit an early passage of claims 38-71 and 73-94 to issuance. Further, Applicants respectfully request that the Examiner telephone the undersigned attorney at (650) 739-3949 prior to issuance of another Office Action should the Examiner be inclined to issue another Office Action rather than the fervently desired Notice of Allowance.

Pursuant to 37 CFR § 1.136(a)(3), the Commissioner is hereby authorized to charge all required fees, including fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Jones Day Deposit Account No. 503013 (order no. 101920-999050).

Respectfully submitted,

Date: December 1, 2004

  
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